Tandem reactions with several heterogeneous catalysts: one-pot vs sequential procedures

José M. Fraile,* Nuria García, Clara I. Herrerías, José A. Mayoral

Instituto de Síntesis Química y Catálisis Homogénea (ISQCH), C.S.I.C.-Universidad de Zaragoza, Facultad de Ciencias, E-50009 Zaragoza, Spain

Corresponding author. +34876553514, jmfraile@unizar.es

Concept

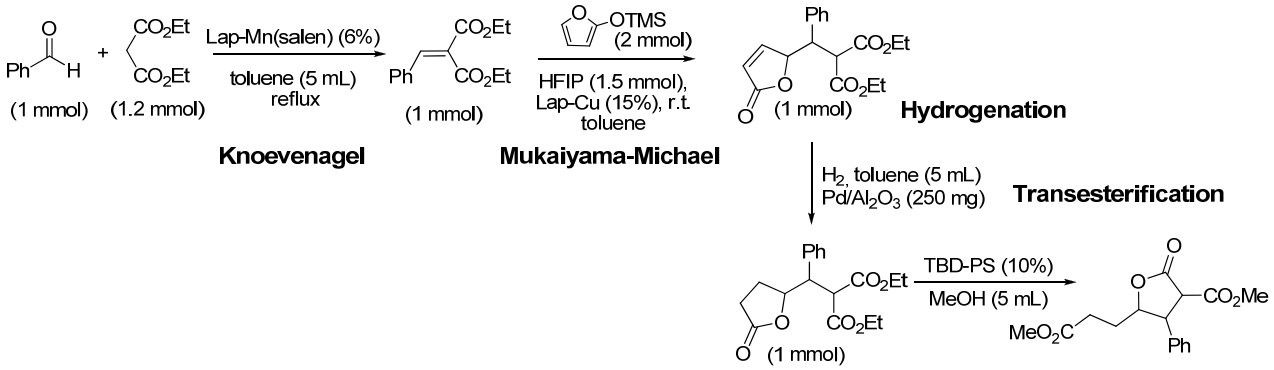
When combining two or more different catalysts for tandem reactions, the use of heterogeneous catalysis can be envisaged in two ways: the design and preparation of bifunctional catalysts [1] or the mixture of two different solid catalysts in "one-pot" processes [2]. If the close proximity of the catalytic sites is not required, the second option is easier, as it does not require especially sophisticated preparation methods. The problem in fine chemicals synthesis is not only the compatibility between catalysts but also, and more importantly, the compatibility of each catalyst with the reagents, reaction conditions, additives, concomitant products and by-products of the other reaction. The sequential methodology, including filtration of each catalyst and use of the crude reaction mixture in the next catalytic step, is the most versatile one, allowing the optimization of the recovery and reuse of each catalyst, as well as the minimization of the separation and purification steps.

Motivations and Objectives

The main objective of this research was to study the compatibility of several catalytic steps in synthetic sequences of fine chemicals synthesis, comparing the scope and limitations of the "one-pot" and sequential methodologies.

Results and Discussion

The compatibilities in a series of reactions, Knoevenagel + Mukaiyama-Michael (even enantioselective) + Hydrogenation + Transesterification, were studied [3,4]. In all the pairs of reactions, the "one-pot" approach revealed some limitations that were solved in the sequential method, but limited to three consecutive reactions. Each catalyst was recovered and reused at the maximum, for example ten times the copper catalyst of the Mukaiyama-Michael reaction or four times in the case of Pd/alumina. The versatility of this methodology has been proved by cross-using the catalysts.



References

[1] R.K. Zeidan, S.-J. Hwang, M.E. Davis, *Angew. Chem. Int. Ed.*, 45 (2006) 6332.
[2] N.T.S. Phan, C.S. Gill, J.V. Nguyên, Z.J. Zhang, C.W. Jones, *Angew. Chem. Int. Ed.*, 45 (2006) 2209.
[3] J.M. Fraile, N. García, C.I. Herrerías, M. Martín, J.A. Mayoral, *ACS Catal.*, 2 (2012) 56.
[4] J.M. Fraile, N. García, C.I. Herrerías, J.A. Mayoral, *Catal. Sci. Technol.*, 3 (2013) 436.

Acknowledgement. Financial support from the Spanish Ministerio de Economía y Competitividad (Project CTQ2011-28124) and the Diputación General de Aragón (E11 Group co-financed by the European Regional Development Funds) is gratefully acknowledged.